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TOWNSEND and TOWNSEND a
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ASSISTANT COMMISSIONER FOR PATENTS
BOX PATENT APPLICATION
Washington, D.C. 20231

EW LLP

RULE 60

Atty. Docket #

528X-00050

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Date of Deposit

25 Jun 96

9-996

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Sir:

This is a request under 37 CFR 1.60 for filing a

[] Continuation [x] Division

of application No. 08/168,904, filed December 15, 1993, which is a continuation of 07/624,114, filed December 6, 1990, which is a continuation-in-part of 07/362,901, filed June 7, 1989 and US Patent 5,143,854, filed March 7, 1990.

of (list each inventor) Stephen P.A. Fodor, Dennis W. Solas and William J. Dower

for Computer Analysis Of Hybridization Data For Base-Checking The Sequence Of A Target Nucleic Acid Molecule

The application papers **FILED HEREWITH** (specification, claims, originally filed drawing(s) and oath or declaration) are a true copy of the prior application.

[] Please amend the specification by inserting before the first line the sentence:

--This is a [] Continuation [x] Division

of application No. _____ filed _____.

[x] A preliminary amendment is enclosed.

[] Formal drawings are enclosed.

[] An Information Disclosure Statement under 37 CFR 1.97 is enclosed.

[] A verified statement to establish status under 37 CFR 1.9 and 37 CFR 1.27 [] is enclosed, or [] was filed in the above identified parent application.

[] Enclosed is a petition to extend time to respond.

[] Please record the enclosed assignment to _____.

[x] The prior application is assigned to Affymax Technologies N.V.

[x] Please cancel claim(s) 11-25

Claims as Filed, Less any Cancelled Claims

	(Col. 1)	(Col. 2)	
FOR:	NO. FILED	NO. EXTRA	
BASIC FEE			
TOTAL CLAIMS	16	-20 =	*0
INDEP CLAIMS	2	-3 =	*0
[] MULTIPLE DEPENDENT CLAIM PRESENTED			

SMALL ENTITY

RATE	FEE	OR
	\$375	OR
x11 =	\$	OR
x39 =	\$	OR
+125 =	\$	OR
TOTAL	\$	OR

**OTHER THAN A
SMALL ENTITY**

RATE	FEE	OR
	\$750	OR
x22 =	\$	OR
x78 =	\$	OR
+250 =	\$	OR
TOTAL	\$750	OR

* If the difference in Col. 1 is less than zero, enter "0" in Col. 2

Please charge Deposit Account No. 20-1430 as follows:

[x] Filing fee

\$ 750

[X] Any additional fees associated with this paper or during the pendency of this application

[] The issue fee set in 37 CFR 1.18 at or before mailing of the Notice of Allowance, pursuant to 37 CFR 1.311(b).

[] A check for \$ _____ is enclosed.

1 extra copy of this sheet is enclosed.

Respectfully submitted,

TOWNSEND and TOWNSEND and CREW LLP

John R. Storella
Reg. No. 32,944

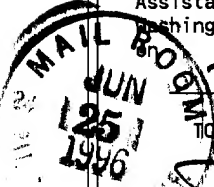
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Washington, D.C. 20231,

PATENT

Attorney Docket No. 16528X-000560



TOWNSEND and TOWNSEND and CREW

By

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

STEPHEN P.A. FODOR ET AL.

Serial No.: Not Assigned

Filed: Herewith

For: SEQUENCING BY HYBRIDIZATION)
OF A TARGET NUCLEIC ACID TO)
A MATRIX OF DEFINED)
OLIGONUCLEOTIDES)

Examiner: Not Assigned

Art Unit: Not Assigned

PRELIMINARY AMENDMENT

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please enter the following amendments before
substantive review of the application.

IN THE TITLE:

Please delete the title (cover page, page 1 and page 143) and
insert therefor:

-- COMPUTER ANALYSIS OF HYBRIDIZATION DATA FOR BASE-CHECKING THE
SEQUENCE OF A TARGET NUCLEIC ACID MOLECULE --

IN THE SPECIFICATION:

On page 1, please delete the first paragraph and insert therefor:
-- This application is a divisional application of Fodor et al.,
Serial No. 08/168,904, filed December 15, 1993, which is a
continuation of Fodor et al., Serial No. 07/624,114, filed
December 6, 1990, now abandoned, which is a continuation in part
application of commonly assigned patent applications Pirrung et

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al., Serial No. 07/362,901, filed June 7, 1989, now abandoned; and Pirrung et al., (1992) U.S. Pat. No. 5,143,854, which are hereby incorporated herein by reference. Additionally commonly assigned applications Barrett et al., Serial No. 07/435,316, filed November 13, 1989, now abandoned; and Barrett et al., (1993) U.S. Pat. No. 5,252,743 are also incorporated herein by reference. Additional applications Pirrung et al., Serial No. 07/624,120, now abandoned, and Dower et al., Serial No. 07/626,730, which are also commonly assigned and filed on December 6, 1990 are also hereby incorporated herein by reference. --

On page 1, line 31, please delete "the"; on line 39, please insert --of-- after "sequence".

On page 3, line 11, please change "VLSIPS" to --VLSIPS™ Technology--; please insert after "VLSIPS™ Technology" --(Very Large Scale Immobilized Polymer Synthesis)--.

On page 3 before the paragraph starting on line 16, please insert the following paragraph: --According to one aspect of the masking technique, the invention provides an ordered method for forming a plurality of polymer sequences by sequential addition of reagents comprising the step of serially protecting and deprotecting portions of the plurality of polymer sequences for addition of other portions of the polymer sequences using a binary synthesis strategy.--

On page 6, line 13, please delete "are".

On page 7, line 22, please delete "upon".

On page 8, line 4, please change "VLSIPS" to --VLSIPS™ Technology--; on line 5, please delete the word "peptide" and insert the word --nucleotide--; on line 6, please change "VLSIPS" to --VLSIPS™ Technology--; on line 7, please delete the word "dipeptide" and insert the word --nucleotide--; on line 8, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 12, line 11, please change "VLSIPS Substrates" to --VLSIPS™ Technology--; on line 15, please change "(VLSIPS)" to --(VLSIPS™)--; on line 35, please delete "U.S.S.N. 07/492,462

(VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--.

On page 13, line 6, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on lines 6-7, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned-- and please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 30, please insert in the blank spaces --07/624,120, now abandoned--; please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 31, please insert in the blank spaces after "U.S.S.N." --Dower et al. (1995) U.S. Pat. No. 5,427,908--; on lines 31-32, please delete "attorney docket number 11509-16 (sequencing by synthesis)".

On page 14, line 28, after "112:", please delete "6997" and insert --6397--; please insert --6399-- in the blank space after "6997".

On page 15, line 11, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on lines 14-15, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned-- and please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 20, line 12, after "07/362,901" insert --, now abandoned -- and please delete "(VLSIPS parent)" and please delete "U.S.S.N. 07/492,462" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 13, please delete (VLSIPS CIP)" and also delete "(caged biotin parent)" and delete "Serial No. 07/612,671" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--; on line 14, please delete "(caged biotin CIP)"; on line 36, after "07/362,901" insert --, now abandoned--; on line 37, delete "U.S.S.N. 07/492,462" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854-- and please delete "(VLSIPS parent)"; on line 37, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on line 37, please delete "(VLSIPS CIP)"; on lines 37-38, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 21, line 11, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 11-12, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 22, line 3, please change "statistically" to --statistical--; on line 24, please change "Khropko" to --Khrapko--.

On page 23, line 12, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 24, line 24, please insert --the-- after "that".

On page 26, line 30, please change "way," to --way--.

On page 31, line 27, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 27-28, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 33, line 14, after "07/435,316" insert --, now abandoned-- and please delete "(caged biotin parent)" and delete "Serial No. 07/612,671" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--; on line 15, please delete '(caged biotin CIP) ".

On page 34, line 14, please change "affixed" to --affixing--; please insert --them-- before the phrase "to a definable position"; on line 16, after "07/362,901" insert --, now abandoned--; on lines 16-17, please delete "(VLSIPS parent)"; on line 17, delete "Serial No. 07/492,462" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; and please delete "(VLSIPS CIP)".

On page 35, line 4, please insert --through the-- after "particularly"; on line 9, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 10, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 10-11, please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 11, please delete "U.S.S.N. 07/612,671 (caged biotin CIP)" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--; on line 16, please delete "U.S.S.N. 07/492,462" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 17, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on line 17, please delete "(VLSIPS

CIP)"; on lines 17-18, please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 30, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 31, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 31-32, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 36, line 9, please change "are" to --is--; on line 21, please insert in the blank spaces --07/624,120, now abandoned--; please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 32, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on line 33, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 37, line 12, please change "converse" to --confer--; on line 30, in the blank space after "6333-" please insert --6335--; on line 31, please insert in the blank space --196--.

On page 38, line 15, please insert --the-- before "target".

On page 39, line 14, please change "it will" to --will allow the probe to--; on line 16, please change "close" to --closely--.

On page 42, line 21, please insert --such-- before "that"; on line 26, please insert --such-- before "that"; on line 31, please change "VLSIPS" to --VLSIPS™ Technoloy--; on line 35, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 41, line 22, delete "arylammonium" and insert --alkylammonium --; line 29, delete "arylammonium" and insert --alkylammonium --.

On page 42, lines 37-38, delete "U.S.S.N. 07/492,462" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--.

On page 43, line 9, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on line 9, please delete "(VLSIPS CIP)"; on lines 9-10, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 47, line 38, please delete "length of the".

On page 48, line 12, please change "individual" to --individually--; on line 38, please insert in the blank spaces after "U.S.S.N." --07/626,730--.

On page 48, line 38 and page 49, line 1, please delete "attorney docket number 11509-26 (sequencing by synthesis)".

On page 49, line 12, in the blank space after "341-" please insert --347--.

On page 50, line 26, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 51, line 4, please change "VLSIPS" to --VLSIPS™ Technology--; on line 12, please change "complex, it" to --complex. It--.

On page 52, line 13, please delete the first occurrence of "expressed".

On page 55, line 3, please insert --and-- after "susceptibilities,".

On page 56, line 7, please change "fingerprinted" to --fingerprinting--; please change "as in" to --an--; on line 8, please change "mosaism" to --mosaicism--.

On page 58, line 4, please delete the sentence "Again, the target sequences may be desired to be fragmented"; please insert the sentence --Again, it may be desirable to fragment the target sequences.--

On page 60, line 19, please change "VLSIPS" to --VLSIPS™ Technology--; on line 33, please delete the second occurrence of "the".

On page 62, line 3, please insert --a-- after "provides"; on line 10, please change "to define" to --in defining--; on line 20, please change "as" to --are--.

On page 63, line 8, please change "upon" to --by--; on line 29, please change "amendable" to --detectable--; on line 38, please change "present" to --presently available--.

On page 64, line 1, please change "screen" to --screens--; on line 17, please change "also is" to --is also--; on lines 33-34, please delete "U.S.S.N. 07/492,462" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 34, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned-- and please delete "(VLSIPS CIP)"; on lines 34-35, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 65, line 3, please change "VLSIPS" to --VLSIPS™ Technology--; on line 9, please delete "U.S.S.N. 07/462,492 (VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 10, please insert in the blank spaces --07/624,120, now abandoned--; please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 66, line 36, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 36-37, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 67, line 14, please change "then" to --them--; on line 33, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 68, line 1, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 2, please insert in the blank spaces --07/624,120, now abandoned-- and please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 7, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 7-8, please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 33, please delete "U.S.S.N. 07/492,462 (automated VLSIPS)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 34, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 34-35, please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 38, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 70, line 2, please insert --,-- after "Fig. C"; on line 6, please change "anaines" to --amines--.

On page 71, line 24, please change "have been" to --include, for example--.

On page 73, line 12, please insert --,-- after "functionalized"; on line 13, please insert --:-- after "(see example below)"; on line 33, please change "group" to --groups--; on line 34, please insert --:-- after "acetate".

On page 74, line 3, please change "." to --:--; on line 16, please change "Related to" to --With respect to--; on line 30, please change "." to --:--.

On page 75, line 4, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on line 5, please delete "attorney docket number 11509-28"; on line 21, after "07/435,316" insert --, now abandoned--; on lines 21-22, please delete "(caged biotin parent)"; on line 22, please delete "U.S.S.N. 07/612,671 (caged biotin CIP)" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--; on line 32, please change "VLSIPS" to --VLSIPS™ Technology--; on line 34, please change "standard VLSIPS" to --"standard VLSIPS™ Technology"--; on lines 34-35, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned-- and please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 77, line 2, please delete "in our labs"; on line 7, please change "Brosystems" to --Biosystems--.

On page 78, line 27, please delete "U.S.S.N. 07/612,671 (caged biotin CIP)" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--.

On page 79, line 31, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 81, line 12, please insert --be-- after "may"; on line 33, please change "Cell" to --In addition to cell--.

On page 82, line 11, please change "VLSIPS" to --VLSIPS™--; on line 19, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 84, line 27, please delete ")".

On page 86, line 30, please change "ficoerythrin" to --phycoerythrin--; on line 32, please change "primary" to --primarily--.

On page 89, line 16, please delete "U.S.S.N. 07/649,642 (VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 17, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 17-18, please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 25, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 25-26, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 90, line 21, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 21-22, please

delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 36, please insert --a-- between "of" and "vast".

On page 91, line 7, please delete "up".

On page 94, line 29, please change "VLSIPS" to --VLSIPS™ Technology--; on line 31, please change "simply" to --simplify--.

On page 95, line 15, please insert --to-- after "adjacent".

On page 96, line 20, please insert --for-- after "sequentially".

On page 97, line 6, please delete "of".

On page 98, line 26, please change "VLSIPS" to --VLSIPS™--; on lines 28-29, please delete "Serial No. 07/612,671 (caged biotin CIP)" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--; on line 34, please change "aa" to --a--.

On page 100, line 12, please change "An" to --In--.

On page 101, line 10, please change "preventative" to --preventive--.

On page 103, line 38, please delete "(VLSIPS parent)" and add --, now abandoned-- after "1989"; on line 39, please delete please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert --Pirrung et al. (1992) U.S. Pat. No. 5,143,854--; on line 40, after "07/435,316" insert --, now abandoned--; and please delete "(caged biotin)"; on line 41, please delete "Serial No. 07/612,671 (caged biotin CIP)" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--; on line 43, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 43-44, please delete "attorney docket number 11509-28 (automated VLSIPS)"; on line 45, please insert in the blank spaces --07/626,730--; on lines 45-46, please delete "attorney docket number 11509-26 (sequencing by synthesis)".

On page 104, line 34, please change "0-nitrovertryl" to --0-nitroveratryl--; on line 35, please change "0-nitrovertryl" to --0-nitroveratryl--.

On page 105, line 31, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 107, line 5, please insert --to-- after "added"; on line 13, please delete "a".

On page 111, line 34, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--"; on line 35, please insert in the blank spaces after "U.S.S.N." --07,624,120, now abandoned--; on lines 35-36, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 112, line 23, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--"; and please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 23-24, please delete "attorney docket number 11509-28 (automated VLSIPS)".

On page 114, lines 21-22, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--"; on line 22, please insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 22-23, please delete "attorney docket number 11509-28".

On page 115, lines 10-11, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--"; on line 23, insert in the blank spaces after "U.S.S.N." --07/624,120, now abandoned--; on lines 23-24, please delete "attorney docket number 11509-28"; on line 36, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--".

On page 116, line 8, please change "durapore" to "--DuraporeTM--".

On page 117, lines 15-16, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--";

On page 118, line 14, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--"; on line 22, please change "NOVC" to "--NVOC--"; on line 29, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--".

On page 120, line 8, please delete "that"; on line 35, please delete "U.S.S.N. 07/492,462 (VLSIPS CIP)" and insert "--Pirrung et al. (1992) U.S. Pat. No. 5,143,854--".

On page 124, line 26, after "07/435,316" insert "--, now abandoned--"; on line 27, please delete "(caged biotin parent)";

on lines 27-28, please delete "U.S.S.N. 07/612,671 (caged biotin CIP)" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--.

On page 126, line 2, please change "are" to --is--.

On page 127, line 3, please delete please delete "U.S.S.N. 07/612,671 (caged biotin CIP)" and insert --Barrett et al. (1993) U.S. Pat. No. 5,252,743--.

On page 131, line 4, please insert --and-- after "recognition".

On page 133, line 2, please insert --to-- after "environment".

On page 134, line 7, please change "her" to --their--.

On page 135, line 37, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 136, line 22, please change "VLSIPS" to --VLSIPS™ Technology--.

On page 144, please delete the paragraph starting on line 15 with "This application", and ending on line 30 with "herein by reference".

IN THE CLAIMS:

Amend the claims as follows:

Cancel claims 11-25 without prejudice to pursue these claims in this application or other applications claiming priority hereon.

Add new claims 26-31 as follows:

-- 26. (New) A method of identifying nucleotide differences between the sequence of a target nucleic acid and the sequence of a reference nucleic acid comprising:

- a) providing a substrate having at least 1000 different oligonucleotide probes of known sequence at known locations, attached at a density of at least 10,000 probes per square cm;
- b) ~~exposing~~ ^{contacting} the target nucleic acid ^{with} ~~to~~ the oligonucleotide probes attached to the substrate under conditions for high fidelity complementary hybridization;

10 c) determining which oligonucleotide probes have hybridized
11 with the target nucleic acid; and

12 d) using a computer to (i) compare the sequence of the
13 reference nucleic acid with the sequences of the oligonucleotide
14 probes that have hybridized with the target nucleic acid and (ii)
15 identify the nucleotide differences between the sequence of the
16 target nucleic acid and the sequence of the reference nucleic
17 acid.

1 27. (New) The method of claim 26 wherein the
2 substrate is produced by the process of:

3 i) providing a substrate having sites protected with
4 photosensitive protective groups;

5 ii) selectively irradiating portions of the substrate
6 with light to remove said photoprotective groups and expose said
7 sites;

8 iii) attaching a nucleotide to the site, said
9 nucleotide protected with a photosensitive protective group; and

10 iv) repeating steps ii) and iii) so as to attach to the
11 substrate at least 1000 different oligonucleotide probes of known
12 sequence at known locations.

1 28. (New) The method of claim 26 further comprising
labeling the target nucleic acid with a fluorescent label.

1 29. (New) The method of claim 28 wherein the
2 oligonucleotide probes that have hybridized with the target
3 nucleic acid are determined by detecting the fluorescent label.

1 30. (New) The method of claim 26 wherein the density
2 of different probes of known sequence is at least 100,000 per
3 square centimeter.

1 31. (New) The method of claim 26 wherein the density
2 of different probes of known sequence is at least 1,000,000 per
3 square centimeter. --

REMARKS

Applicants have canceled claims 11-25 in favor of new claims 26-31 which are presented for examination.

This application is a divisional of co-pending application serial number 08/168,904, filed December 15, 1993. In that application, Applicants had elected Group II, claims 11-25. In an Office Action dated June 3, 1996, the Examiner withdrew Applicants' amended claims 26, 27, 29, 30, 32 and 33 on the ground that the claims included different process steps than the claims of group II and, therefore, constituted a distinct invention (Group III). Accordingly, Applicants are presenting here the claims of Group I, claims 1-10 and Group III in new claims 26-31.

Applicants also amended the title to more closely reflect the claimed invention. Applicants' amendments to the specification reflect amendments made in the priority application and do not constitute new matter.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (415) 326-2400.

Respectfully submitted,



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